Acta Microbiologica et Immunologica Hungarica, 50 (4), pp. 453–457 (2003)

VANCOMYCIN-RESISTANT *ENTEROCOCCUS FAECALIS* COLONIZATION DURING RECOVERY FROM *NEISSERIA MENINGITIDIS* CEREBROSPINAL MENINGITIS

CASE REPORT

M. KNAUSZ[1], B. GARTNER[1], I. FÖMÖTÖR[1], Á. GHIDÁN[2], K. KAMOTSAY[2] and F. ROZGONYI[2]*

[1]Clinical Microbiology, Intensive Care Unit and Plastic Surgery Department, Petz Aladár County Teaching Hospital, Győr, Hungary
[2]Institute of Medical Microbiology, Semmelweis University, Budapest, Hungary

(Received: 18 February 2003; accepted: 23 April 2003)

A 19-year-old man had been admitted to the Hospital because of septic shock and large scale suffusions all over the body. The pathogen had proved to be *Neisseria meningitidis* serogroup C. In his stabilization period two superinfectious attacks arose. One of them was a bacteremia, caused by a vancomycin-sensitive *Enterococcus faecium*. The second was a wound infection in his deep colliquating necrotised tissue of the heel. Vancomycin-resistant *Enterococcus faecalis* (VREF) was isolated from this lesion with some Gram-negative oppurtunistic pathogens. The strain contained the *vanA* gene. After systemic and topical treatment, furthermore plastic surgical interventions the patient recovered. This is the second report on VREF from Hungary colonizing/infecting a patient with an underlying disease.

Keywords: vancomycin resistance, enterococcus, colonization, long hospitalization

Introduction

During the last decade vancomycin-resistant *Enterococcus* (VRE) infections have arisen as major problems throughout the world. Most common sites of these infections are the blood stream, decubital and diabetic wounds and the urinary tract [1]. Multiple-resistant enterococci have been recovered from patients

* Corresponding author; Phone/fax: +36 1 210-2959, E-mail: rozfer@net.sote.hu

hospitalized for a long period of time, and receiving glycopeptides and/or broad spectrum antibiotics, mainly cephalosporins and carbapenems [1]. Sometimes it is difficult to define the pathogenic importance of such enterococci in mixed infections, but may, however, cause therapeutic problems, prolong the length of hospitalisation, and indicate the potential risk of transferring vancomycin-resistance to other nosocomial pathogens.

Case report

We report here the case of a 19-year-old male, who was admitted to the Intensive Care Unit (ICU) of the Hospital with life-threatening infection. There was no important disease in his medical history. At admission he suffered from high fever, leucocytosis, septic-shock and metabolic acidosis; body temperature, 38.5–39.7 °C; blood pressure, 80/50 Hgmm; erythrocyte sedimentation rate (ESR), 25 mm/h; white blood cell (Wbc), 11.3×10^9/l (neutrophils 80%, monocytes 10%, lymphocytes 8%, eosinophils 2%); thrombocytes, 16×10^9/l; C-reactive protein content, 210 mg/l; tachycardia, oliguria, blood pH, 7.21; extensive suffusions on the extremities.

Except disorientation, no other neurological disorder was observed. Cerebrospinal fluid (CSF) analysis included: total protein, 1.2 g/l; cell count, 63/µl polymorphonuclear leucocytes; Gram-negative diplococci were seen microscopically. Both the antigen detection by Wellcogen-kit and the cultivation of the CSF together with the positive blood cultures in Vital bottles (bioMérieux) confirmed *Neisseria meningitidis* serogroup C to be the causative agent. Meropenem (3×2 g/day) was given intravenously with complex anti-shock therapy. Intubation and mechanical ventillation were needed for 6 days. Repeated negative CSF and blood cultures indicated the decline of the disease. On the 10^{th} day the patient was shivering and got high fever again (body temperature, 39–39.5 °C; Wbc, 14.6×10^9/l). Vancomycin-sensitive *Enterococcus faecium* was grown from the blood cultures and crural wounds. (Using rapid ID 32 Strep system – bioMérieux for identification and disk diffusion methods for susceptibility testing.)

Vancomycin therapy (4×500 mg/day) was given. Repeated blood cultures were negative. After treatment the patient was transferred to the plastic surgery department, because 2/3 parts of his skin was necrotized and 4^{th} and 5^{th} toes on both sides were dry gangreneous. Necrotomy was done and the lesions were covered by porcine xenograft.

After a few days of the operation he became again febrile (37.4–38.5 °C), his ESR rose. Cerebral and abdominal CT scan showed no focal lesions. Blood cultures were negative.

His right 5th and left 4th–5th toes were amputated. Vancomycin-resistant *Enterococcus faecalis* was recovered along with *Pseudomonas aeruginosa*, *Morganella morganii*, *Enterobacter cloacae* from deep necrotic tissue of the heel (10^5 CFU/ml). The *Enterococcus faecalis* strain was ampicillin-sensitive, gentamicin-intermediate with a minimal inhibitory concentration (MIC) of 256 mg/l vancomycin and 32 mg/l teicoplanin using E test (AB Biodisk) (Table 1). PCR amplification with *vanA* primers resulted in a *vanA* gene product from the strain. The patient received simultaneusly ampicillin (4×500 mg/day) and gentamicin (2×80 mg/day) intramuscularly followed by an ownskin alloplastic surgery. He was discharged home after a total period of 2 and half months of hospitalization.

Swab cultures from environmental surfaces, and rectal swabs of the patient and staff members were screened for VRE simultaneously on Columbia agar (bioMérieux) and Enterococcosel agar with 30 μg vancomycin disk and Mueller–Hinton blood agar containing 6 mg/l vancomycin. The staff and the environment of the ward were negatives. The patient's faeces yielded an *E. faecium* strain with a MIC of 12 mg/l vancomycin and 2 mg/l teicoplanin (Table 1). PCR amplification showed none of the *vanA*, *vanB* and *vanC* genes in the strain.

Table I

Antibiotic sensitivity/resistance patterns of *Enterococcus* strains isolated from the patient during the course of infection

Antibiotic	*E. faecium* from blood, disk diffusion	*E. faecalis* from wound, ATB Strep., E-test	E. faecium from faeces ATB Strep., E-test
Penicillin	R	I	R
Ampicillin	R	S	R
Erythromycin	R	R	S
Lincomycin	R	R	R
Tetracycline	R	R	S
Co-trimoxazole	R	R	S
Rifampicin	ND	S	S
Vancomycin	S	256 mg/l	12 mg/l
Teicoplanin	S	32 mg/l	2 mg/l
Streptomycin HCl	ND	I	I
Kanamycin HCl	ND	R	I
Gentamicin HCl	I	I	I

R = resistant; I = intermediate; S = sensitive; ND = not determined

Discussion

Nosocomial enterococcal infections have recently amounted to about 10% for all nosocomial infections. Most of them are probably endogenous, arising from the patient's gut flora. The exogenous infections related to poor hospital hygiene, arising from the environmental contamination or from the hands of medical staff [1]. Leclercq at al. [2] reported the first VRE strain in 1988 in France. Since then, VRE strains have become common worldwide [3, 4, 5, 6]. Risk factors for their acquisition include prior use of antimicrobials such as glycopeptides, third generation cephalosporins and antianaerobic drugs, severe illness and long length of hospitalisation [7]. The Centers for Disease Control reported VRE nosocomial infections in the U.S. hospitals to increase from 0.3% in 1989 to 7.9% in 1993 [8]. In contrast, in European centers the frequency of VRE nosocomial isolates are about 1% [5]. In Hungary the first report of VRE was described in 2000 by Ghidán et al [9]. It seems that the patients in Europe acquire VRE from the community and import it into the hospitals [1, 10]. VRE selection in the community may partly be due to avoparcin, a glycopeptide analog used for about 20 years as a supplement to animal feeds in many western European countries and in Australia but not in the U.S. [11]. The preopearative oral use of vancomycin for patients undergoing colon surgery may be another selective factor. In our case the personal source of the glycopeptide-resistant *E. faecalis* strain as a member of the superinfecting flora could not be revealed since neither the patient nor the ward staff harbored such a strain in their faeces. The patient, however, had all predisposing factors to acquire VRE (septic shock, cerebrospinal meningitis, meropenem and vancomycin therapy, long hospitalization). Nevertheless, the main predisposing factor for VRE colonization and persistence was the lack of cellular defense in the necrotised skin tissue.

This is the second report of VRE in Hungary documented by molecular genetic methods, indicating a real danger of the spread of high-level vancomycin-resistance among enterococci and from them to other nosocomial pathogens. Further studies are needed in order to examine the source of VRE and their spread among patients.

Acknowledgements. This work was supported in parts by the Council of Health Sciences, Hungary, grant No. ETT-T-146/99, and by the National Scientific Research Fund (OTKA), Hungary, grant No. T 032473.

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